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MORGAN, LEWIS & BOCKIUS, LLP. 3300 HILLVIEW AVENUE PALO ALTO, CA 94304			MUTSCHLER, BRIAN L	
			ART UNIT	PAPER NUMBER
			1753	
DATE MAILED: 07/08/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/728,723

Applicant(s)

YENGOYAN ET AL.

Examiner

Brian L. Mutschler

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-15, 17-33, 35, 38-75 and 77-134 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-15, 17-33, 35, 38-75 and 77-134 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 May 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

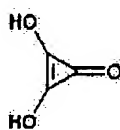
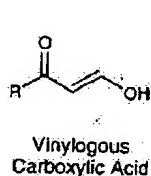
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

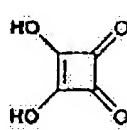
- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 20040512.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION**Comments**

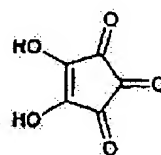
1. The scope of the claimed vinylogous carboxylic acid compound is still unclear. Applicant has provided the reference of Perez et al. in support of the apparent definition provided in the present specification. Perez et al. define a vinylogous carboxylic acid compound as "the juxtaposition of a hydroxy group in conjugation with a carbonyl." Perez et al. provide examples of relatively simple compounds, including the following:



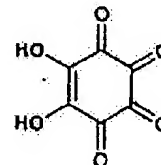
Deltic Acid



Squaric Acid

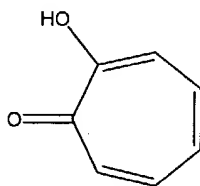
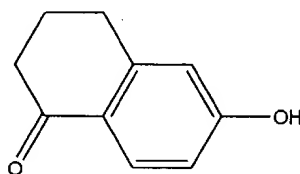


Croconic Acid

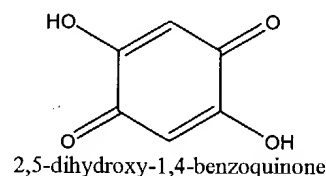


Rhodizonic Acid

The definition of Perez et al. is in accord with the generic definition provided in the specification, which states that "vinylogous carboxylic acid compounds of the present invention are defined as compounds containing one or more enol function groups in conjugation with one or more carbonyl functional groups through one or more carbon-carbon or carbon-nitrogen double bonds" (see page 6 at lines 14-17). Examples of such compounds within this definition include the following compounds disclosed in the present application:

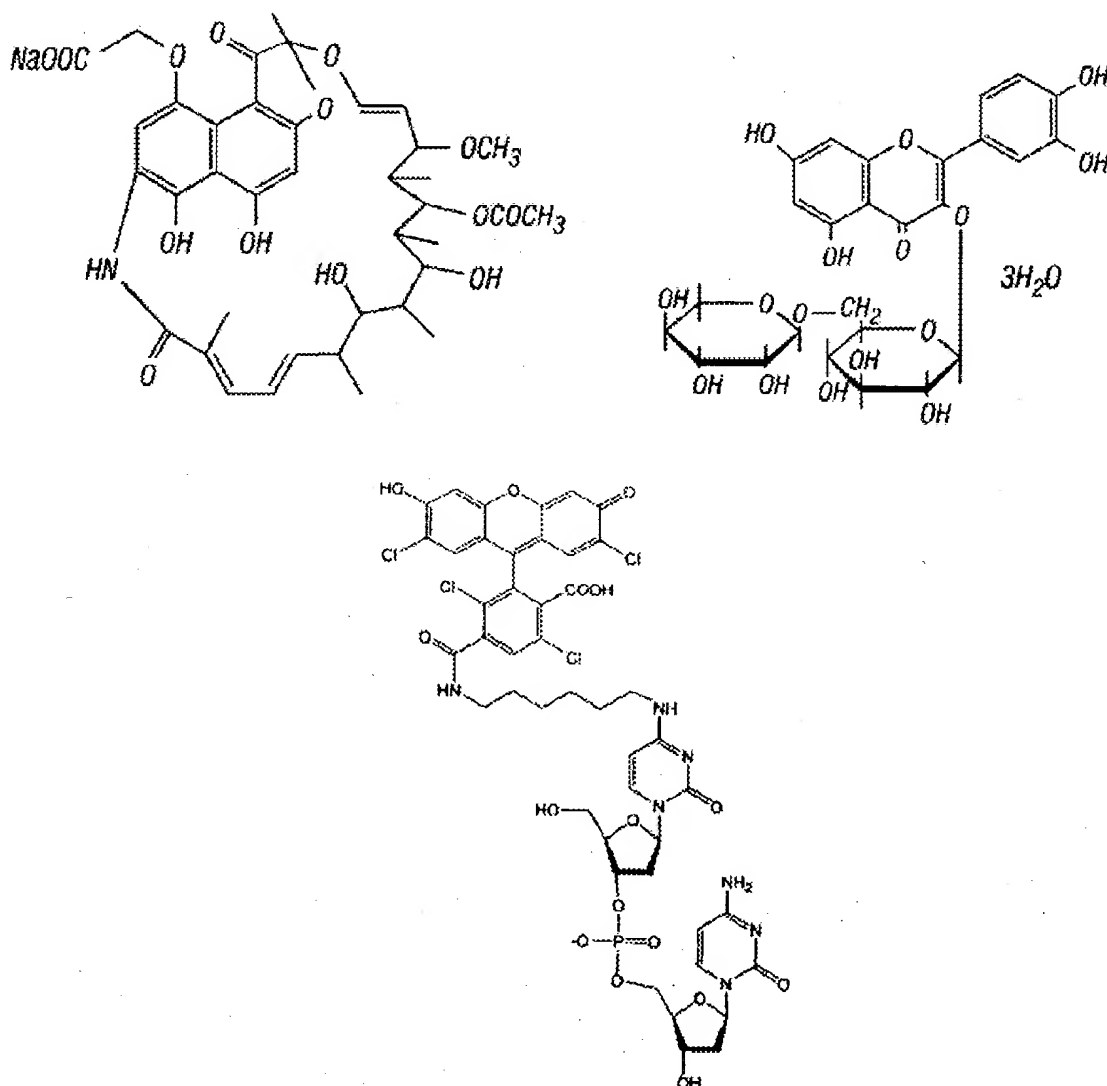


2-hydroxy-2,4,6-cycloheptatrienone



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While the above examples are fully enabled by the disclosure, the scope encompasses a substantially greater and more diverse class of compounds that are not apparent to one skilled in the art, and are thus not enabled. The definition assigned by Perez et al. and adopted by Applicant includes significantly more complex compounds than those disclosed by either Perez et al. and Applicant. Such complex compounds include the following compounds disclosed in U.S. Pat. No. 6,322,980 and U.S. Pat. No. 6,331,235:



As can be seen in each of the complex compounds pictured above, each compound has at least one hydroxy or enol group in conjugation with a carbonyl group through one or more carbon-carbon or carbon-nitrogen double bonds. However, the present specification does not suggest that such complex molecules could be used for the specified use. While such compounds fit within the general description of a vinylogous carboxylic acid compound, it would not be readily apparent from the disclosure that such compounds would function in the desired manner. Furthermore, at what point does the compound lose its acidic functionality due to distance between the carbonyl group and the enol?

Additionally, the present claims further introduce ambiguity with respect to the definition of vinylogous carboxylic compounds. Claim 1 is not limited to compounds having one or more enol functional groups in conjugation with one or more carbonyl functional groups through one or more carbon-carbon or carbon-nitrogen double bonds. The compounds encompassed by claim 1 are not so limited until claim 2. Therefore, it is unclear what compounds Applicant intends to encompass by within vinylogous carboxylic acid compounds. This discrepancy between the disclosure and the claims is further shown by the apparent substitution of vinylogous carboxylic acid derivatives in the scope of vinylogous carboxylic acid compounds. For example, as recited in claims 17, 18, 127, and 128, the probe includes amide or ester derivatives of vinylogous carboxylic acid compounds. As indicated in the specification, it appears that such derivatives are considered equivalents or substitutes to vinylogous carboxylic acid compounds (see page 10 at lines 11+). However, these compounds do not fit within the

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definition of a vinylogous carboxylic acid compound as provided by Perez et al. and the present specification. As seen in the compounds recited in claims 127 and 128, there is no hydroxy or enol group conjugated with a carbonyl group. Since the claim language and the specification treat such derivatives as substitutes for the vinylogous carboxylic acid compounds, such probes including the derivatives cannot be considered vinylogous carboxylic acid compounds.

The difficulty in defining the scope of the claimed vinylogous carboxylic acid compounds is further exacerbated by the relatively rare use of the phrase to define such compounds. A search of the patent database (including U.S., Japanese, and European patents) yields a total of six occurrences of the phrase "vinylogous carboxylic acid", with none of the references providing any indication of the compounds included by the phrase. An internet search using the Google search engine (<http://www.google.com>) provides similar results. The Google search only provides six websites that include the phrase "vinylogous carboxylic acid(s)".

In light of the discrepancies between the examples provided by Perez et al. and the present disclosure and the vast scope of the compounds encompassed by the generic definition of vinylogous carboxylic acid compounds, the scope of the claims exceeds the limited group of vinylogous carboxylic acid compounds enabled by the present specification.

2. The objections to the drawings, specification, and claims has been overcome by Applicant's amendment.

3. Applicant has made numerous changes to the claims in the amendment received May 12, 2004. These changes are addressed below. Applicant's cancellation of claims 10, 16, 34, 36, 37, and 76, and the addition of claims 91-134 in the amendment received May 12, 2004, is noted.

Drawings

4. The drawings were received on May 12, 2004. These drawings are acceptable.

Claim Objections

5. Claims 17, 18, 52, 53, 73, 74, 89, 90, and 127-134 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 17 and 18 recite the limitation "wherein said probe includes a cationic enol [ester/amide] derivative of a vinylogous carboxylic acid compound" in lines 2-4 of each claim. The claim language suggests that the derivatives are substitutions of the vinylogous carboxylic acid compounds comprising the probe of claim 1. Since the vinylogous carboxylic acid compound of claim 1 is replaced with the derivatives of claims 17 and 18, the claims no longer further limit the limitations of claim 1. The same applies to claims 127 and 128. (As indicated in the specification, the derivatives are alternatives to vinylogous carboxylic acid compounds, and as such, the derivatives are

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not used in conjunction with the vinylogous carboxylic acid compounds, but as substitutes.)

Claims 52, 53, 73, 74, 89, and 90, recite the limitation "wherein said vinylogous carboxylic acid compound is a cationic enol [ester/amide] derivative a vinylogous carboxylic acid" in lines 1-3 of each claim. In light of Perez et al.'s definition of a vinylogous carboxylic acid compound, the ester/amide derivatives are not vinylogous carboxylic acid compounds. Therefore, the substitution of the derivatives for the vinylogous carboxylic acid compounds does not further limit the preceding claims. The same applies to dependent claims 129-134.

6. Claims 2-9, 11-13, 51, 104, 127, and 128 are objected to because of the following informalities:

- a. In claims 2-9 and 11-13, the term "compounds" should be changed to --compound-- to reflect the changes made to independent claim 1.
- b. In claim 51 at line 1, please change "The probe" to --The method--.
- c. In claim 104 at line 1, it appears that the preamble "The method of claim 96" should be changed to --The method of claim 103--.
- d. In claims 127 and 128 at line 1, please change "The solution" to --The background electrolyte solution--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-9, 11-15, 17-33, 35, 38-75, and 77-134 are rejected under 35

U.S.C. 112, first paragraph, because the specification, while being enabling for vinylogous carboxylic acid compounds having one or more enol functional groups in conjugation with one or more carbonyl functional groups through one or more carbon-carbon or carbon-nitrogen double bonds, does not reasonably provide enablement for any vinylogous carboxylic acid compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The specification clearly defines the vinylogous compounds of the invention as compounds having one or more enol functional groups in conjugation with one or more carbonyl functional groups through one or more carbon-carbon or carbon-nitrogen double bonds (see page 6 at lines 14-17; page 10 beginning at line 11). Since the specification clearly defines vinylogous carboxylic acid compounds as having those features, the scope of the claims exceeds the scope of the disclosure, comprising compounds not envisioned or taught by the Applicant.

Additionally, the specification only discloses relatively simple compounds. As explained above, the definition of a vinylogous carboxylic acid compound provided by Perez et al. and the instant disclosure comprises a very large class of compounds.

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While satisfying the general definition of a vinylogous carboxylic compound, complex compounds (e.g., compounds that have multiple functional groups or compounds where the hydroxy group is separated from the carbonyl group by a large number of conjugated bonds) would not have the same properties as the simpler compounds disclosed. Therefore, one skilled in the art would not be enabled to use any compound fitting the definition.

Furthermore, the disclosure and claims recite ester and amide derivatives of vinylogous carboxylic acid compounds. While these compounds are derivatives of vinylogous carboxylic acid compounds, they are not vinylogous carboxylic acid compounds as defined by Applicant in the disclosure. What is the definition of an ester or amide derivative of a vinylogous carboxylic acid compound? An ester or amide derivative can have an ester or amide functionality at any position within the compound. The examples shown in the disclosure replace the enol functionality with the ester or amide functionality. Therefore, such derivatives no longer fall within the definition of a vinylogous carboxylic acid compound.

9. Claims 1-9, 11-15, 17-19, 35, 91, 92, 94-97, and 121-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claims 1, 121, 123, and 125 recite limitations wherein a probe comprises a vinylogous carboxylic acid compound, wherein the vinylogous carboxylic acid compound is not tropolone. This limitation presents new matter that was not disclosed in the original specification. As disclosed and originally claimed, tropolone is a preferred vinylogous carboxylic acid compound (see page 7 at lines 8+). Therefore, the express exclusion of tropolone is not supported by the original disclosure and is new matter.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 14, 17-19, 33, 52, 53, 73, 74, 89, 90, and 104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "is vinylogous carboxylic acid UV-chromophore" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim. The UV-chromophore was never introduced, so any reference to it is indefinite. The same applies to claim 35.

Claim 17 recites the limitation "said probe includes a positively charged cationic ester derivative of a vinylogous carboxylic acid compound" in lines 2-4. This limitation is indefinite because unclear what the actual probe comprises. Claim 1 recites that the probe comprises one or more vinylogous carboxylic acid compounds, and claim 17

recites that the probe includes a derivative of such compounds. What does the probe comprise? The same applies to claim 18.

Claims 52, 53, 73, 74, 89, and 90, recite the limitation "wherein said vinylogous carboxylic acid compound is a cationic enol [ester/amide] derivative a vinylogous carboxylic acid" in lines 1-3 of each claim. This limitation is indefinite because such derivatives do not fall within the class of compounds defined by Perez et al. as vinylogous carboxylic acid compounds.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 20-22, 32, 33, 35, 60-62, 72, 75, 77, 78, 88, 91, 106, 114, 123, and 125 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukushi et al.

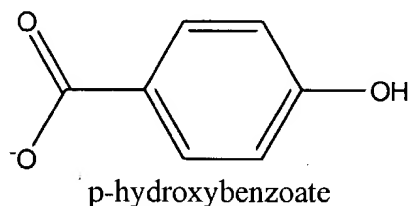
("Determination of ascorbic acid in vegetables by capillary zone electrophoresis," Journal of Chromatography A, 772 (1997) p. 313-320).

Fukushi et al. disclose a method and apparatus using capillary electrophoresis to detect ascorbic acid (3-oxo-L-gulofuranolactone) (abstract). The electrolyte comprises ascorbic acid in a buffer at a pH of 9.2 (see page 314). The apparatus further comprises a UV-Vis absorbance detector and a power source, which is inherently required to perform electrophoresis (see page 314 "2.1 Apparatus").

Since Fukushi et al. teach all of the limitations recited in the instant claims, the reference is deemed to be anticipatory. The functional language and preambles of the instant limit the instant claims only insofar as the prior art must be capable of being used in the recited manner.

14. Claims 121, 123, and 125 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al. (U.S. Pat. No. 5,366,601).

Jones et al. disclose a method, apparatus and kit for performing capillary electrophoresis to separate UV-absorbing or UV-transparent anions comprising a capillary with a solution containing an aromatic carboxylate such as p-hydroxybenzoate, which is compound within the definition of a vinylogous carboxylic acid compound (col. 6, lines 27-51).



An electric current is applied across the capillary to move and separate the anions and the anions are detected by UV-Vis spectroscopy (col. 5, lines 1-10). The detection is by either direct or indirect UV detection since the method may be used for both UV-absorbing and UV-transparent anions (col. 5, lines 11-25). The solution may also be provided in a kit (col. 3, lines 23-29).

Since Jones et al. teach all of the limitations recited in the instant claims, the reference is deemed to be anticipatory.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 1-3, 13-15, 19, 38, 105, 113, 124, and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukushi et al. ("Determination of ascorbic acid in vegetables by capillary zone electrophoresis," Journal of Chromatography A, 772 (1997) p. 313-320).

Fukushi et al. disclose a method and apparatus using capillary electrophoresis to detect ascorbic acid (abstract). The electrolyte comprises ascorbic acid in a buffer at a pH of 9.2 (see page 314). Fukushi et al. further demonstrate the well-known laboratory practice of dilution of samples, wherein a 5.7 mM solution of ascorbic acid is diluted to 0.3 mM or less (see page 314, "2.2 Reagents").

The electrolyte solution of Fukushi et al. differs from the instant invention because Fukushi et al. do not disclose that the ascorbic acid is present at a concentration of 2-5 mM.

As Fukushi et al. demonstrate, the concentration of the ascorbic acid is controlled by dilution (see page 314, "2.2 Reagents").

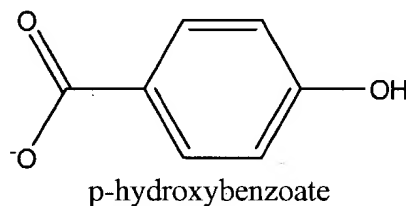
It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the concentration of the ascorbic acid in the

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solution of Fukushi et al. because the concentration of a compound in an electrolyte is a variable dependent on many experimental factors, and the adjustment of concentration to satisfy the desired needs of an experiment is one of the basic fundamentals of laboratory practice.

17. Claims 1-4, 14, 15, 19, 91, 92, 94, 95, 122, 124, and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601).

Jones et al. disclose a method, apparatus and kit for performing capillary electrophoresis to separate UV-absorbing or UV-transparent anions comprising a capillary with a solution containing an aromatic carboxylate such as p-hydroxybenzoate, which is compound within the definition of a vinyllogous carboxylic acid compound (col. 6, lines 27-51).



An electric current is applied across the capillary to move and separate the anions and the anions are detected by UV-Vis spectroscopy (col. 5, lines 1-10). The detection is by either direct or indirect UV detection since the method may be used for both UV-absorbing and UV-transparent anions (col. 5, lines 11-25). The solution may also be provided in a kit (col. 3, lines 23-29).

The solution is maintained at a pH of about 7.5 to about 8.5, but can also be less than 3 (col. 6, lines 4-26).

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The solution may further comprise an electroosmotic flow modifier such as cetyltrimethylammonium bromide (col. 5, line 26 to col. 6, line 3).

The solution of Jones et al. differs from the instant invention because Jones et al. does not disclose that the concentration of the vinylogous carboxylic acid compound is 2-5 mM, as recited in claims 1, 122, and 126.

The concentration of a detection compound in a solution in such a method as taught by Jones et al. is dependent on several experimental factors, including the sensitivity of the compound and the detector, the concentration of the target molecule in the solution, the presence of other compounds in the solution, etc. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the concentration of the vinylogous carboxylic acid compound in the solution of Jones et al. to use any concentration suitable for experimental conditions.

18. Claims 5-9, 11-13, 17, 18, 127, and 128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601), as applied above to claims 1-4, 14, 15, 19, 91, 92, 94, 95, 122, 124, and 126, further in view of supporting evidence provided by Allinger et al. ("Chromophoric Groups" and "Conjugated Systems," Organic Chemistry, 2nd Ed., p. 764-768 (1976)).

Jones et al. teach the limitations recited in claims 1-4, 14, 15, 19, 91, 92, 94, 95, 122, 124, and 126 of the instant invention, as explained above.

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Jones et al. teach indirect detection of anions separated by capillary electrophoresis using a vinylous carboxylic acid compound such as p-hydroxybenzoate (col. 6, lines 27-51). Jones et al. further teach that "a range of highly UV-absorbing carrier electrolytes covering the range of ionic mobilities of all inorganic anions and other low molecular weight species is of practical interest" (col. 6, lines 40-44).

The teachings of Jones et al. differ from the limitations recited in the instant invention because they do not disclose the other compounds recited in the instant claims.

As is shown by Allinger et al., carbon-carbon double bonds and carbonyl groups are chromophoric groups that are highly UV-absorbing (see Table 29.1). Furthermore, conjugation results in an intense increase in UV absorption (page 765).

The claimed compounds have similar functional groups, chemical structures, and molecular weights as the compounds taught by Jones et al. Since the claimed compounds are highly UV-absorbing, these compounds would be included within the class of compounds disclosed by Jones et al. as being "of practical interest." One skilled in the art would expect these compounds to have similar UV-absorptivities, mobilities, and interactions as the compounds disclosed by Jones et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have substituted the claimed compounds for the compounds taught by Jones et al. because the selection of a known material based on

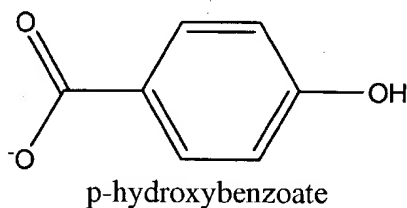
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its suitability for its intended use supports a prima facie obviousness determination.

See MPEP 2144.07.

19. Claims 20-23, 35, 38-42, 54-56, 58-63, 75, 77-79, 93, 98-102, 105-110, and 113-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601) in view of Macka et al. ("Changes in Electrolyte pH Due to Electrolysis during Capillary Zone Electrophoresis," Anal. Chem., 70, p. 743-749 (February 15, 1998)).

Jones et al. disclose a method, apparatus and kit for performing capillary electrophoresis to separate UV-absorbing or UV-transparent anions comprising a capillary with a solution containing an aromatic carboxylate such as p-hydroxybenzoate, which is compound within the definition of a vinylogous carboxylic acid compound (col. 6, lines 27-51).



An electric current is applied across the capillary to move and separate the anions and the anions are detected by UV-Vis spectroscopy (col. 5, lines 1-10). The detection is by either direct or indirect UV detection since the method may be used for both UV-absorbing and UV-transparent anions (col. 5, lines 11-25). The solution may also be provided in a kit (col. 3, lines 23-29).

The solution is maintained at a pH of about 7.5 to about 8.5, but can also be less than 3 (col. 6, lines 4-26).

The solution may further comprise an electroosmotic flow modifier such as cetyltrimethylammonium bromide (col. 5, line 26 to col. 6, line 3).

The capillary allows for anion flow and is lined with a polyimide permitting reverse electroosmotic flow (col. 9, lines 3-18; col. 10, line 65 to col. 11, line 19).

Jones et al. further discloses that capillary electrophoresis may be performed using gels or liquids, including buffers (col. 1, lines 29-43). However, Jones et al. does not disclose the use of a buffer as recited in claims 20, 39, 60, and 75, or that the buffer is a tris base, an amine, or an organic base, as recited in claims 93, 100, 108, and 116.

Macka et al. teach that "it is well known that electrolysis of the background electrolyte (BGE) caused by the applied separation voltage is an accompanying phenomenon in electrophoresis" and that the electrolysis causes localized pH changes that have significant effects on the separation (see page 743). Macka et al. teach the use of Tris buffer to prevent changes in the pH (page 744).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the solution of Jones et al. to use a Tris buffer as taught by Macka et al. because a buffer would prevent localized pH changes that negatively affect the separation.

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The solution of Jones et al. differs from the instant invention because Jones et al. does not disclose that the concentration of the vinylogous carboxylic acid compound is 2-5 mM, as recited in claims 38, 102, 105, and 113.

The concentration of a detection compound in a solution in such a method as taught by Jones et al. is dependent on several experimental factors, including the sensitivity of the compound and the detector, the concentration of the target molecule in the solution, the presence of other compounds in the solution, etc. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the concentration of the vinylogous carboxylic acid compound in the solution of Jones et al. to use any concentration suitable for experimental conditions.

20. Claims 20-23, 29, 32, 33, 35, 38-42, 48, 51, 54-63, 69, 72, 75, 77-79, 85, 88, 91, 94, 95, 98, 101, 102, 105, 106, 109, 110, 113, 114, 117, and 118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oehrle ("Controlled changes in selectivity of cation separations by capillary electrophoresis using various crown-ether additives", J. Chromatogr. A 745 (1996) 87-92) in view of Jones et al. (U.S. Pat. No. 5,128,005).

Oehrle teaches a method for separating ions by capillary electrophoresis using an electrolyte containing tropolone, a resonance-stabilized aromatic vinylogous carboxylic acid having a tautomeric keto-enol form (page 88). The method further includes the detection of ions in the sample by indirect UV detection (page 87). A

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power supply would inherently be used to provide the necessary potential for electrophoresis to occur.

The probe is capable of detecting ions of various molecular weights, including potassium (see Figure 2).

The concentration of tropolone in the electrolyte is 3.0 mM (page 88).

The capillary is a polyamide fused silica capillary (page 87).

Oehrle also teaches that the pH of the electrolyte may be altered to achieve a separation (page 87).

The electrolyte of Oehrle differs from the instant invention because Oehrle does not teach the use of a buffer, as recited in claims 20, 60, and 75; the ions are anions, as recited in claims 56-58; the use of an EOF modifier, as recited in claims 59, 94, 95, 101, 109, 110, 117, and 118; and the pH is in the range of about 7 to 10, as recited in claims 91, 98, 106, and 114.

Buffers are commonly used in chemical analysis because they maintain the pH of the solution constant, which is especially important in electrophoresis where the applied potential causes electrolysis of the electrolyte. For example, Jones et al. teach a method of analyzing analytes using capillary electrophoresis and indirect detection, wherein the electrolyte comprises a buffer (col. 1, lines 30-42). Jones further teaches that the pH may be 7.5 to 8.5, and may be modified to a desired level (col. 5, lines 45-49).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the electrolyte of Oehrle to use a buffer as taught by Jones et al. because a buffer would maintain the pH of the electrolyte at a constant value.

Jones et al. also teach that flow modifiers, including cetyltrimethylammonium bromide, may be used to control the flow of the electrolyte (col. 5, lines 5-8).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the electrolyte of Oehrle to use a flow modifier as taught by Jones et al. because flow modifiers allow the flow of the electrolyte to be controlled.

While Oehrle teaches the detection of cations, Jones et al. teach that similar methods and solutions may be used to detect anions using vinylogous carboxylic acid compounds such as p-hydroxybenzoate (col. 5, line 50 to col. 6, line 6).

It would have been obvious to one skilled in the art to use a method as taught by Oehrle to detect anions as taught by Jones et al. because Jones et al. teaches that capillary electrophoresis with UV-absorbing compounds can be similarly used to detect anions.

21. Claims 24-28, 30, 31, 43-47, 49, 50, 52, 53, 64-68, 70, 71, 73, 74, 80-84, 86-90, and 129-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oehrle

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("Controlled changes in selectivity of cation separations by capillary electrophoresis using various crown-ether additives", J. Chromatogr. A 745 (1996) 87-92) in view of Jones et al. (U.S. Pat. No. 5,128,005), as applied above to claims 20-23, 29, 32, 33, 35, 38-42, 48, 51, 54-63, 69, 72, 75, 77-79, 85, 88, 91, 94, 95, 98, 101, 102, 105, 106, 109, 110, 113, 114, 117, and 118 of the instant invention, and further in view of supporting evidence provided by Allinger et al. ("Chromophoric Groups" and "Conjugated Systems," Organic Chemistry, 2nd Ed., p. 764-768 (1976)).

Oehrle and Jones et al. teach the limitations recited in claims 20-23, 29, 32, 33, 35, 38-42, 48, 51, 54-63, 69, 72, 75, 77-79, 85, 88, 91, 94, 95, 98, 101, 102, 105, 106, 109, 110, 113, 114, 117, and 118 of the instant invention, as explained above.

Oehrle teaches indirect detection of cations separated by capillary electrophoresis using a vinylogous carboxylic acid compound such as tropolone (page 87).

Jones et al. teach indirect detection of anions separated by capillary electrophoresis using a vinylogous carboxylic acid compound such as p-hydroxybenzoate (col. 5, line 50 to col. 6, line 6). Jones et al. further teach that "a range of highly UV-absorbing carrier electrolytes covering the range of ionic mobilities of all inorganic anions and other low molecular weight species is of practical interest" (col. 5, lines 63-67).

The teachings of Oehrle and Jones et al. differ from the limitations recited in the instant invention because they do not disclose the other compounds recited in the instant claims.

As is shown by Allinger et al., carbon-carbon double bonds and carbonyl groups are chromophoric groups that are highly UV-absorbing (see Table 29.1). Furthermore, conjugation results in an intense increase in UV absorption (page 765).

The claimed compounds have similar functional groups, chemical structures, and molecular weights as the compounds taught by Oehrle and Jones et al. Since the claimed compounds are highly UV-absorbing, these compounds would be included within the class of compounds disclosed by Jones et al. as being "of practical interest." One skilled in the art would expect these compounds to have similar UV-absorptivities, mobilities, and interactions as the compounds disclosed by Oehrle and Jones et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have substituted the claimed compounds for the compounds taught by Oehrle and Jones et al. because the selection of a known material based on its suitability for its intended use supports a prima facie obviousness determination. See MPEP 2144.07.

22. Claims 24-31, 43-53, 64-74, 80-90, and 129-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601) in view of Macka et al. ("Changes in Electrolyte pH Due to Electrolysis during Capillary Zone Electrophoresis," Anal. Chem., 70, p. 743-749 (February 15, 1998)), as applied above to claims 20-23, 35, 38-42, 54-56, 58-63, 75, 77-79, 93, 98-102, 105-110, and 113-118, and further in view of supporting evidence provided by Allinger et al. ("Chromophoric Groups" and "Conjugated Systems," Organic Chemistry, 2nd Ed., p. 764-768 (1976)).

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Jones et al. and Macka et al. teach the limitations recited in claims 20-23, 35, 38-42, 54-56, 58-63, 75, 77-79, 93, 98-102, 105-110, and 113-118 of the instant invention, as explained above.

Jones et al. teach indirect detection of anions separated by capillary electrophoresis using a vinylogous carboxylic acid compound such as p-hydroxybenzoate (col. 6, lines 27-51). Jones et al. further teach that "a range of highly UV-absorbing carrier electrolytes covering the range of ionic mobilities of all inorganic anions and other low molecular weight species is of practical interest" (col. 6, lines 40-44).

The teachings of Jones et al. and Macka et al. differ from the limitations recited in the instant invention because they do not disclose the other compounds recited in the instant claims.

As is shown by Allinger et al., carbon-carbon double bonds and carbonyl groups are chromophoric groups that are highly UV-absorbing (see Table 29.1). Furthermore, conjugation results in an intense increase in UV absorption (page 765).

The claimed compounds have similar functional groups, chemical structures, and molecular weights as the compounds taught by Jones et al. Since the claimed compounds are highly UV-absorbing, these compounds would be included within the class of compounds disclosed by Jones et al. as being "of practical interest." One skilled in the art would expect these compounds to have similar UV-absorptivities, mobilities, and interactions as the compounds disclosed by Jones et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have substituted the claimed compounds for the compounds taught by Jones et al. and Macka et al. because the selection of a known material based on its suitability for its intended use supports a prima facie obviousness determination. See MPEP 2144.07.

23. Claims 96 and 97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601), as applied above to claims 1-4, 14, 15, 19, 91, 92, 94, 95, 122, 124, and 126, and further in view of Vigh et al. (U.S. Pat. No. 6,511,850).

Jones et al. discloses a solution having the limitations recited in claims 1-4, 14, 15, 19, 91, 92, 94, 95, 122, 124, and 126 of the instant invention, as explained above.

The solution of Jones et al. differs from the instant invention because Jones et al. does not disclose the use of organic solvents in the buffer, wherein the organic solvents may include such compounds as methanol, ethanol, or acetone.

Vigh et al. disclose a background electrolyte for use in capillary electrophoresis, and teach that suitable electrolytes include aqueous buffers, a mixed solvent system including an organic solvent, or an organic solvent buffer (col. 7, lines 31-45). Organic solvents include methanol and ethanol (col. 7, lines 31-45).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the electrolyte of Jones et al. to include an organic solvent as taught by Vigh et al. because Vigh et al. teach that electrolytes with organic

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solvents are suitable background electrolytes for capillary electrophoresis and the substitution of an equivalent solution for a known suitable purpose is deemed obvious to one skilled in the art.

24. Claims 103, 104, 111, 112, 119, and 120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (U.S. Pat. No. 5,366,601) in view of Macka et al. ("Changes in Electrolyte pH Due to Electrolysis during Capillary Zone Electrophoresis," Anal. Chem., 70, p. 743-749 (February 15, 1998)), as applied above to claims 20-23, 35, 38-42, 54-56, 58-63, 75, 77-79, 93, 98-102, 105-110, and 113-118, and further in view of Vigh et al. (U.S. Pat. No. 6,511,850).

Jones et al. discloses a solution having the limitations recited in claims 103, 104, 111, 112, 119, and 120 of the instant invention, as explained above.

The solution of Jones et al. differs from the instant invention because Jones et al. does not disclose the use of organic solvents in the buffer, wherein the organic solvents may include such compounds as methanol, ethanol, or acetone.

Vigh et al. disclose a background electrolyte for use in capillary electrophoresis, and teach that suitable electrolytes include aqueous buffers, a mixed solvent system including an organic solvent, or an organic solvent buffer (col. 7, lines 31-45). Organic solvents include methanol and ethanol (col. 7, lines 31-45).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the electrolyte of Jones et al. to include an organic solvent as taught by Vigh et al. because Vigh et al. teach that electrolytes with organic

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solvents are suitable background electrolytes for capillary electrophoresis and the substitution of an equivalent solution for a known suitable purpose is deemed obvious to one skilled in the art.

Response to Arguments

25. Applicant's arguments with respect to claims 1-90 have been considered but are moot in view of the new ground(s) of rejection.

26. The rejection of the claims has been modified in light of Applicant's amendment to the claims.

27. With respect to the rejection of claims 20-23, 29, 32-38, 54, 56, 58, 59, and 76 over Oehrle in view of Jones et al. (US '005), Applicant has argued, "One of ordinary skill in the art would not have been motivated to combine the teachings of Oehrle and Jones because Oehrle is directed to separations of cations, whereas Jones is principally directed to separation of anions, and the teaching that pertains to cations utilizes compounds that are very different from tropolone" (see page 36 of Applicant's response). This argument is not persuasive because even if Jones et al. principally teaches the separation of anions, Jones et al. still disclose the separation of cations. Furthermore, the level of one of ordinary skill in the art is relatively high. The use of buffers in electrophoretic separations is well known. In addition, the selection of appropriate solutions and compounds for the separation of either anions or cations would be readily apparent to one of ordinary skill in the art. The teachings of Oehrle and Jones et al. have a high degree of similarity and minor differences particular to the

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separation of anions as opposed to cations are well within the skill of the ordinary artisan. As noted above, the scope of compounds encompassed by Perez et al.'s definition of vinylogous carboxylic acid compounds is extremely large. The compounds disclosed by Oehrle and Jones et al. fall within the definition of vinylogous carboxylic acid compounds. It is further noted that the majority of the claims merely recite a solution or method for the detection of ions. Therefore, the scope of the claims encompasses the detection of anions and cations.

28. It is noted that independent claims 1, 20, 75, and 125 are very broad and include very few actual limitations. For example, claim 1 merely requires a vinylogous carboxylic acid compound in solution at a concentration. The majority of compounds satisfying the definition of a vinylogous carboxylic acid compound are used in solution. Therefore, almost any compound falling within the definition will anticipate and/or obviate the instant claims.

Conclusion

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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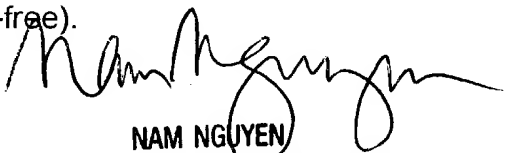
mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian L. Mutschler whose telephone number is (571) 272-1341. The examiner can normally be reached on Monday-Friday from 7:30am to 4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BLM
July 2, 2004


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